

Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Claims 39-47 and 49-51 are pending in this application. Claims 39-43 remain rejected. Claims 44-47 and 49-51 have been allowed. The pending and allowed claims have been amended for clarity to remove references to Figures and now refer to the SEQ ID NOs alone; their entry is respectfully requested. The rejections to claims 39-43 are respectfully traversed.

Claim Rejections – 35 USC § 112, First Paragraph, Enablement

Claims 39-43 are rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement.

Previously, Applicants had submitted reasons why the inflammation observed in Assay #64: the skin vascular permeability assay was not due to "an irritant" or an allergic response, especially since the PRO331 molecule was injected into a **non-presensitized** animal, which is the case of ran irritation or an allergic reaction. However, the Examiner maintains that this "assay merely establishes that the substance applied is an irritant". The Examiner also maintains that "the results remain a preliminary one, necessitating substantial further research to determine how to use the compound". For the reasons described below, Applicants respectfully traverse.

Applicants hereby file an executed Declaration by Sherman Fong, Ph.D., an expert in the field of immunology, that discusses the skin vascular permeability assay, its results and shows this assay and its modifications has been widely used in the art to identify various well-established proinflammatory molecules like blood coagulation factor XIII, VEGF, etc. Such proinflammatory molecules are not considered irritants. As Dr. Fong says,

"Proinflammatory molecules can directly or indirectly cause vascular permeability by causing immune cells to exit from the blood stream and move to the site of injury or infection".

Further, an exhibit of a positive reaction is shown in Exhibit I. Applicants add that in this assay, the results were further analyzed by histopathological examination to rule out inflammation due to endothelial cell damage or mast cell degranulation. Hence, the vascular permeability observed were not due to histamine release or endothelial cell damage. The utilities for PRO331, based on a positive score in the skin vascular permeability assay would readily be understood, appreciated and accepted by those skilled in the art at the effective filing date. Further, one skilled in the art

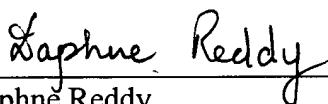
would know how to make and use the invention without undue experimentation based on the instant disclosure and the advanced knowledge in the art regarding this assay. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-1618P2C44). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

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